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Evaluation of the combined measurement uncertainty in isotope dilution by MC-ICP-MS

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Abstract The combination of metrological weighing, the measurement of isotope amount ratios by a multicollector inductively coupled plasma mass spectrometer (MC-ICP-MS) and the use of high-purity reference materials are the cornerstones to achieve improved results for the amount content of lead in wine by the reversed isotope dilution technique. Isotope dilution mass spectrometry (IDMS) and reversed IDMS have the potential to be a so-called primary method, with which close comparability and well-stated combined measurement uncertainties can be obtained.

This work describes the detailed uncertainty budget determination using the ISO-GUM approach. The traces of lead in wine were separated from the matrix by ion exchange chromatography after HNO_3/H_2O_2 microwave digestion. The thallium isotope amount ratio ($n(^{205}Tl)/n(^{203}Tl)$) was used to correct for mass discrimination using an exponential model approach. The corrected lead isotope amount ratio $n(^{206}Pb)/n(^{208}Pb)$ for the isotopic standard SRM 981 measured in our laboratory was compared with ratio values considered to be the least uncertain. The result has been compared in a so-called pilot study "lead in wine" organised by the CCQM (Comité Consultatif pour la Quantité de Matière, BIPM, Paris; the highest measurement authority for analytical chemical measurements).

The result for the lead amount content k(Pb) and the corresponding expanded uncertainty U given by our laboratory was:

- $k(Pb)=1.329\times10^{-10}$ mol g^{-1} (amount content of lead in wine)
- $U[k(Pb)]=1.0\times10^{-12}$ mol g^{-1} (expanded uncertainty $U=k\times u_c$, $k=2$)

The uncertainty of the main influence parameter of the combined measurement uncertainty was determined to be the isotope amount ratio $R_{206,B}$ of the blend between the enriched spike and the sample.

Keywords Isotope dilution · Measurement uncertainty · Lead · Multicollector inductively coupled plasma mass spectrometry · Isotope amount ratio · ISO-GUM

Abbreviations X sample · Y enriched isotopic spike material · Z isotopic assay standard · N_A Avogadro constant · k_X amount content of the sample X (cf. ref. [5] for quantity k) · k_Y amount content of the spike Y · k_Z amount content of the assay standard Z · m_X mass of the sample X · m_Y mass of the spike Y (used for R_B) · m_Z mass of the assay standard Z · m'_Y mass of the spike Y (used for R'_B) · n amount of substance · R corrected isotope amount ratio · R' measured isotope amount ratio · R_X isotope amount ratios of the sample · R_Y isotope amount ratio of the spike · R_B isotope amount ratio of the blend X and Y · R'_B isotope amount ratio of the blend Z and Y · R_Z isotope amount ratio of the certified natural material · R_{204} isotope amount ratio $n(^{204}Pb)/n(^{208}Pb)$ · R_{206} isotope amount ratio $n(^{206}Pb)/n(^{208}Pb)$ · R_{207} isotope amount ratio $n(^{207}Pb)/n(^{208}Pb)$ · u_X standard uncertainty of X · u_c combined measurement uncertainty · k coverage factor (not to be confused with amount content) · s standard deviation · U expanded uncertainty · R_{ref} certified isotope amount ratio of the reference material · R_{obs} observed isotope amount ratio of the reference material · Δm mass difference of measured isotope pair · ε mass discrimination correction factor per mass unit · *OIML* Organisation Internationale de la Métrologie Légale · *CCQM* Comité Consultatif pour la Quantité de Matière · *IMEP* International Measurement Evaluation Program

Introduction

Achieving traceability and hence comparability of analytical results is one of the principal challenges in analytical

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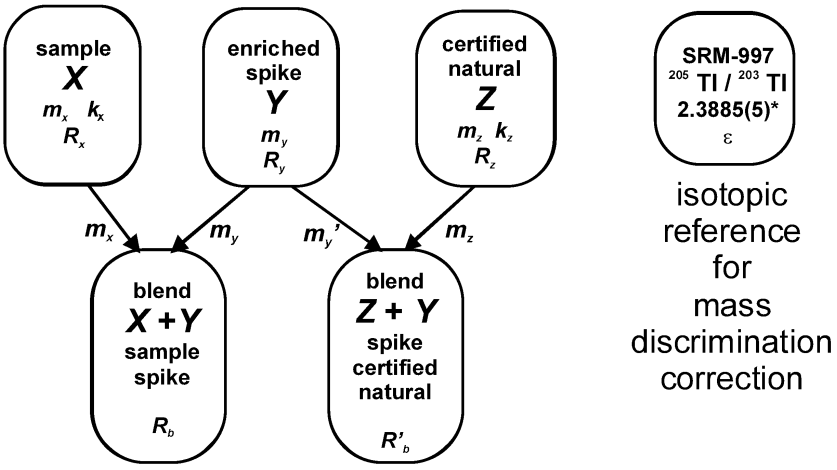

Fig. 1 Principle of reverse isotope dilution mass spectrometry for lead with one reverse step and the corresponding measurand equation for the amount content k of the analyte X. When quadrupol mass spectrometry is applied the last term with the two summations is sometimes considered to be one, therefore the approximation equation. In this work MC-ICP-MS was used and no approximation was applied. *) The reference value was slightly adapted according to internationally published values

$$k_X = k_Z \cdot \frac{m_Y}{m'_Y} \cdot \frac{m_Z}{m_X} \cdot \frac{(R_{206,Y} - R_{206,B})}{(R_{206,B} - R_{206,X})} \cdot \frac{(R'_{206,B} - R_{206,Z})}{(R_{206,Y} - R'_{206,B})} \cdot \frac{\sum_i R_{Xi}}{\sum_i R_{Zi}}$$

$$\cong k_Z \cdot \frac{m_Y}{m'_Y} \cdot \frac{m_Z}{m_X} \cdot \frac{(R_{206,Y} - R_{206,B})}{(R_{206,B} - R_{206,X})} \cdot \frac{(R'_{206,B} - R_{206,Z})}{(R_{206,Y} - R'_{206,B})}$$

chemistry. The combination of metrological weighings and the use of multi-collector inductively coupled plasma mass spectrometry (MC-ICP-MS) enable the analyst to reduce the combined measurement uncertainty of analyte amount content values determined by application of the isotope dilution (ID) method [1, 2]. The principle of reverse IDMS is based on determining isotope amount ratios of natural abundance and isotopically enriched spiked samples (Fig. 1) [3]; the latter are prepared by metrological weighing [4]. The enriched spike amount content has no influence on the measurand in reverse IDMS.

The equation (Eq. 1) for the amount content k [2, 5] of an analyte (lead with ^{208}Pb as the reference isotope and ^{206}Pb as the enriched spike isotope) determined by IDMS with one reverse step can be written as:

$$k_X = k_Z \cdot \frac{m_Y}{m'_Y} \cdot \frac{m_Z}{m_X} \cdot \frac{(R_{206,Y} - R_{206,B})}{(R_{206,B} - R_{206,X})} \cdot \frac{(R'_{206,B} - R_{206,Z})}{(R_{206,Y} - R'_{206,B})} \cdot \frac{(R_{204,X} + R_{206,X} + R_{207,X} + 1)}{(R_{204,Z} + R_{206,Z} + R_{207,Z} + 1)} \quad (1)$$

The following scheme in Fig. 1 shortly illustrates the procedure for the reverse IDMS.

In accordance with the *Guide to the expression of uncertainty in measurement* (ISO-GUM [7]) the combined measurement uncertainty $u_c(k_X)$ (Eq. 2) is calculated using the uncertainty propagation law without consideration of second-order contributions; an abbreviated equation is used therefore:

$$u_c^2(k_X) = \sum_{i=1}^{n} \left(\frac{\partial k_X}{\partial x_i} \right)^2 \cdot u^2(x_i) \quad (2)$$

All the partial derivatives were calculated according to ISO-GUM using the model equation (Eq. 1) for the amount content as a starting point. The different influence parameters and their contribution to the combined measurement uncertainty are identified and quantified. Certain influence parameters are dependent on variables which do not appear directly in the model equation for the measurand. The measured isotope amount ratios are biased and need a correction. A mass discrimination correction factor ε using an exponential model was applied. Apart from mass discrimination as a systematic influence a small signal drift correction was applied to take into account any time-dependent signal variations.

Experimental

Instrumentation

All weighings necessary for the preparation of the mixtures of isotopically enriched spike and the wine sample were performed in a class E2 weighing room with stabilised air temperature and relative air humidity as well as monitored air pressure. All weighings were done on an analytical balance (AT 201 Mettler-Toledo, Greifensee, Switzerland). The balance was regularly checked by the use of class E2 reference weights traced back to the Swiss National Standards References.

All measurements of the different isotope amount ratios were performed using the VG AXIOM MC-ICP-MS (Thermo-Elemental, Winsford, Cheshire, England). The instrument was operated in an air temperature (17±1 °C) stabilised clean hood (class 100) laboratory. Before the high-precision isotope amount ratio measurements were started, the instrument was stabilised for about 1.5 h under normal working conditions until the temperature sensor within the mass spectrometer indicated constant values of ±0.2 K. The air temperature in the room was monitored during the measurements to detect any unacceptable deviation from the target value of 17±1 °C. The lower temperature allows slightly better vacuum conditions in the detector and therefore improves sensitivity of the detection. The MC-ICP-MS operating conditions and a typical image of the signals of a 200 ng g^{-1} lead and 50 ng g^{-1} thallium solution are presented in Table 1 and Fig. 2 respectively. No

Table 1 Analytically relevant operating conditions for VG Axiom MC-ICP-MS

Parameter	Value
RF power (W)	1,250
Plasma Ar gas flow (L min^{-1})	14.0
Auxiliary Ar gas flow (L min^{-1})	0.58
Nebulizer Ar gas flow (L min^{-1})	1.0
Sampling cone material	Ni
Mass resolving power (10% valley) $m/\Delta m$	410
Dwell time (ms)	50
Points per replicate	40
Mass assignment to Faraday cup detectors	
Tl	203 L2
Pb	204 L3
Tl	205 Ax
Pb	206 H1
Pb	207 H2
Pb	208 H3
Aerosol drying unit	CETAC Aridus
Nebulizer type	TH1 concentric
Typical sample uptake rate (µL min^{-1})	100
Air temperature in clean hood for instrument (°C)	17±1

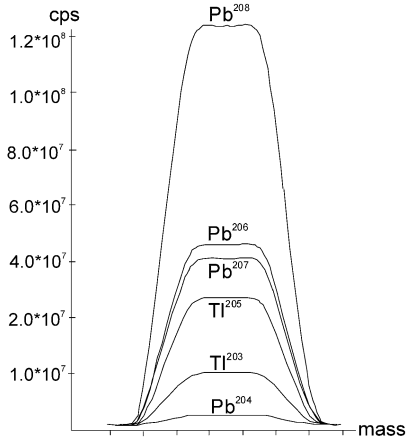

Fig. 2 Typical MC-ICP-MS signals registered for lead with added thallium as internal standard in a cleaned wine sample

dead time correction was necessary as a linear response was due to the Faraday cup detectors.

The analyte solutions were taken up by free aspiration using a TH1 nebuliser (CETAC, Omaha, USA). The analyte sample uptake rate of the nebuliser was about 100 µL min^{-1}. The wet aerosol was dried by an Aridus (CETAC, Omaha, USA) aerosol desolvating system using 3 L min^{-1} argon and 20 mL min^{-1} nitrogen (temperature 160 °C). The system was cleaned for 2 min before every run by aspirating a 2% HNO_3 solution. The dry aerosol was feed to the torch assembly kept at a voltage of 5,000 V. A gain calibration of the multicollector system was performed once a week. Collector efficiency factors were adjusted using Nd (La Jolla), whereby a maximum positive correction of about 100 ppm had to be applied in relation to unity. Faraday cup multicollector detector positions were optimised while a mixture of 200 µg kg^{-1} Pb (SRM 981, NIST) and 50 µg kg^{-1} Tl (SRM 997, NIST) was introduced. Day-to-day variations of the relative multicollector detector positions were in the order of 0.1 mm at maximum.

Isotope amount ratios of Pb and Tl in the wine samples were determined using the following sequence: mixture of 200 µg kg^{-1} Pb (SRM 981, NIST) and 50 µg kg^{-1} Tl (SRM 997, NIST); sample No 1 and 50 µg kg^{-1} Tl (SRM 997, NIST); 200 µg kg^{-1} Pb (SRM 981, NIST) and 50 µg kg^{-1} Tl (SRM 997, NIST); sample No 2 and 50 µg kg^{-1} Tl (SRM 997, NIST)...; 200 µg kg^{-1} Pb (SRM 981, NIST) and 50 µg kg^{-1} Tl (SRM 997, NIST); spiked sample No 1 and 50 µg kg^{-1} Tl (SRM 997, NIST)...SRM 997 thallium isotopic standard was added to the samples. Between each measurement the wash sequence with 2% HNO_3 solution lasted for 2 min.

Sample

The red wine sample was distributed by the IRMM (Geel, Belgium) and used for the CCQM-P12 study which was piloted by IRMM. The IMEP-16 round on the wine sample was organised as well by the IRMM.

Sample decomposition and matrix separation

The wine samples were spiked with an isotopically enriched ^{206}Pb solution (SRM 991, NIST, USA), first by gravimetric dilution of the spike solution and then by adding a defined portion of it to the wine samples. The sample mass was chosen in the range of 5 g and the net weighing value was determined by difference.

The digestion of the wine and spiked wine samples was performed using 8–10 mL of wine, mixed with 1 mL of concentrated, sub-boiled nitric acid and 4 mL of hydrogen peroxide (Baker, Ultrex II) in a Teflon beaker. An adapted temperature program was used for the microwave digestion (MILESTONE mls 1200 mega) to get a controlled decomposition of the organic matrix compounds without loss of solvent.

Matrix separations were performed using home-made polypropylene columns (10-mL volume) loaded with 2 cm^3 of the cation exchange resin Serdolit CHE (Fluka, Switzerland). It was first activated with 50 mL of 2 M HNO_3 to replace all Na^+ cations by H^+ then by neutralising with 40 mL high-purity H_2O to a pH > 3. The sample was carefully loaded onto the column, then 30 mL of a nitric acid solution of pH 3 (±0.1) and 20 mL of pH 2 (±0.1) was added. Finally, 10 mL of a 2% nitric acid solution was used to desorb the lead ions from the column and to obtain 2.5-mL fractions. The lead-containing fractions were combined and used for mass spectrometric isotope ratio determinations.

The assay standard solution was prepared by dissolving a high-purity lead piece (Alfa Aeser, USA) of accurately determined mass with a stated purity of 99.999% (on a metals basis) in 10% freshly distilled nitric acid.

All other dilutions were made gravimetrically with 2% freshly sub-boiled HNO_3 under class 100 clean hood conditions. Sample containers were leached with diluted nitric acid over an extended period of time by placing them on a mechanical shaker.

Measurement

The measurement procedure consists of the weighings for the preparation of the isotopic mixtures, the decomposition of the organic matrix by microwave digestion, the separation of the analyte from the inorganic matrix by a specific ion exchange resin and the precise determination of isotope amount ratios by MC-ICP-MS with a Faraday cup detection system. To keep blank levels low, all manipulations of the samples were performed under class 100 clean room conditions and only high-purity reagents, substances and carefully cleaned equipment were used. All measured isotope amount ratios were corrected for mass discrimination using the isotopic thallium reference material (SRM 997, NIST).

Results and discussion

Mass values and standard uncertainties

For metrological mass determinations the densities of the samples and the references as well as the environmental parameters, which are linked to the air density, need to be known. Therefore an air buoyancy correction has to be applied to the weighing value in order to correct for the main systematic influence. According to ISO-GUM [7] all known, relevant biases demand a correction of the weighing value. Apart from this correction the uncertainty from the air buoyancy is included in the combined uncertainty. The uncertainties of the mass values, under the chosen conditions, have only a secondary influence. Some typical mass values and their uncertainties are listed in Table 2.

Isotope amount ratios, standard uncertainties and combined measurement uncertainty

Three certified isotopic reference materials were used to correct or check the measured isotope amount ratios using an exponential model. Thallium NIST SRM 997 [8] was measured at 50 ng g^{-1} level and used as internal ratio reference. The data from the certificate of NIST SRM 981 (common lead isotopic standard) and literature data [9, 10, 11] were compared with results of our measurements from five independent runs. The equal-atom lead isotopic standard NIST SRM 982 was used as a check at increasing contents (50 ng g^{-1} up to 500 ng g^{-1}).

The values and its uncertainties for R_{204}, R_{206} and R_{207} overlap with the data from the NIST certificate and are comparable to the published values [6, 9, 10, 11]. The uncertainties of the isotope amount ratios (e.g. $R_{206,B}$) are composed of a contribution from the blank value, the external repeatability, the internal precision and the correction of the Faraday detector cup efficiencies. As the internal precision only affects the 10^{-4} to 10^{-5} uncertainty range only the repeatability and the variations of the blank values have to be considered. The uncertainty of the blank value was included using the standard deviation for three independent values from the blank solutions. Minimum and maximum values for all relevant isotope amount ratios were calculated. The difference between the two values were used as uncertainty borders with a symmetric triangular distribution of the mean isotope amount ratio values.

The standard uncertainty of the amount ratio from the spike can be calculated using the values given in the certificate divided by a factor of two, as the coverage factor given in the certificate is two.

Standard uncertainty of the mass discrimination correction factors

As each measured isotope amount ratio was corrected for mass discrimination several uncertainty contributions needed to be taken into account:

- The uncertainty of the certified isotope amount ratio value
- The uncertainty of the measured isotope amount ratio
- The uncertainty originating from signal drift phenomena between one measurement of sample and the next

Starting from an exponential model, the mass discrimination per mass unit ε (Eq. 3) is deduced and is described by the following mathematical relationship [3]:

$$\varepsilon = \frac{\ln\left(\frac{R_{ref}}{R_{obs}}\right)}{\Delta m} \tag{3}$$

By application of the uncertainty propagation law the following expression (Eq. 4) is deduced using the fact that the mass difference Δm of the isotopes involved is considered to be constant with negligible or zero uncertainty ($u(\Delta m) \equiv 0$) (typical values are presented in Table 3):

$$u(\varepsilon) = \sqrt{\left(\frac{\partial \varepsilon}{\partial R_{ref}}\right)^2 \cdot u^2(R_{ref}) + \left(\frac{\partial \varepsilon}{\partial R_{obs}}\right)^2 \cdot u^2(R_{obs}) + u^2\left(\varepsilon\left(R_{drift}\right)\right)} \tag{4}$$

The combined measurement uncertainty has been evaluated by application of the ISO-GUM [7] concept without simplification of the extended expressions for all partial derivatives.

Figure 3 illustrates the result for all influence parameters explicitly and implicitly involved in the model equation for the measurand.

Table 2 Typical uncertainty values of the mass (liquid, PFA bottles) under E2 conditions (OIML)

Mass (g)	Standard uncertainty u (g)	Combined uncertainty u_c(g)	Relative combined uncertainty $u_{c,rel}$
1	1×10^{-4}	0.0001	1×10^{-4}
10	5×10^{-5}	0.0001	8×10^{-6}
50	4×10^{-5}	0.0003	6×10^{-6}
100	3.8×10^{-5}	0.0001	2×10^{-6}

Table 3 Uncertainty values of the components used for the combined uncertainty of the mass discrimination correction factor ε (cf. Eq. (4))

Quantity	Measured or certified value	Standard uncertainty (u)
R_{ref}	2.3885	0.0005
R_{obs}	2.4321	0.00033
Signal drift	–	0.0004
ε	–0.00794	0.0005

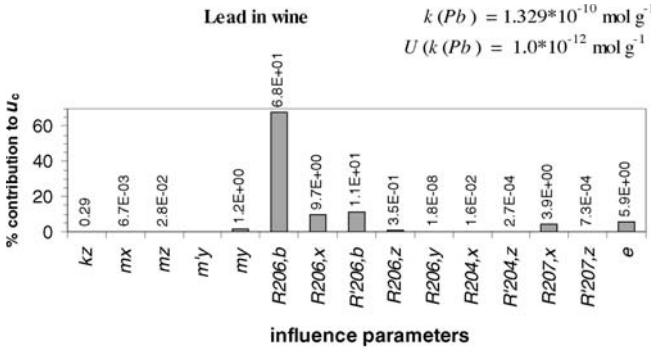

Fig. 3 Relative contributions of the different influence parameters (squared sensitivity factor that is the partial derivative multiplied with the squared standard uncertainty) to the combined squared measurement uncertainty u_c as calculated by application of the ISO-GUM [7] concept

Replicate analysis of the wine samples

The mean of the amount content [$k(Pb)=n(Pb)/m_X$] of lead in wine and the corresponding expanded uncertainty for three measured wine samples and blends (Table 4) were calculated as follows (Eq. 5):

$$k(Pb)=\frac{1}{3}\sum_{i=1}^{3}k(Pb_i)=1.329\times10^{-10}\ \text{mol g}^{-1} \tag{5}$$

A "within-blend" uncertainty contribution was calculated (cf. Eq. 6) by applying the uncertainty propagation law to the expression of the mean [12]:

$$u_{within}[k(Pb)]=\frac{1}{3}\sqrt{u^2[k(Pb_1)]+u^2[k(Pb_2)]+u^2[k(Pb_3)]}$$
$$=7\times10^{-13}\,\text{mol g}^{-1} \tag{6}$$

The standard deviation of the mean (standard deviation divided by $\sqrt{3}$) for the three determined blends was used as an estimate of the "between-blend" uncertainty component $u_{between}=3.5\times10^{-13}$ mol g^{-1} (Table 4).

The "within" and "between" blend uncertainties were combined using the square root of the sum of the squared uncertainties (coverage factor $k = 2$) [12]:

$$U[k(Pb)]=k\cdot\sqrt{u^2_{between}[k(Pb)]+u^2_{within}[k(Pb)]}$$
$$=1\times10^{-12}\,\text{mol g}^{-1} \tag{7}$$

The degree of comparability for metrological laboratories has been shown in the study "lead in wine" which was organised by the "Comité Consultatif pour la Quantité de Matière CCQM, BIPM, Paris, France" (cf. Fig. 4). A traceable reference value and carefully estimated combined measurement uncertainties allows good comparability of results on an international level. The results from certain laboratories in the IMEP-16 study show that given uncertainties do not always fulfil this requirement.

Table 4 Results of the IDMS analysis of three different blends (spiked wine, spiked assay standard)

Blend identification	Amount content $k(Pb)$, sample x (mol g^{-1})	Combined standard uncertainty $u_c(k(Pb))$	
		(mol g^{-1})	(%)
Blend 1	1.325×10^{-10}	6.03×10^{-13}	0.46
Blend 2	1.336×10^{-10}	6.51×10^{-13}	0.49
Blend 3	1.326×10^{-10}	5.90×10^{-13}	0.43
Mean $k(Pb)$	1.329×10^{-10}	$U[k(Pb)]=1.0\times10^{-12}$ mol g^{-1}	
$s[k(Pb)]_{mean}$ (%)	0.26	–	

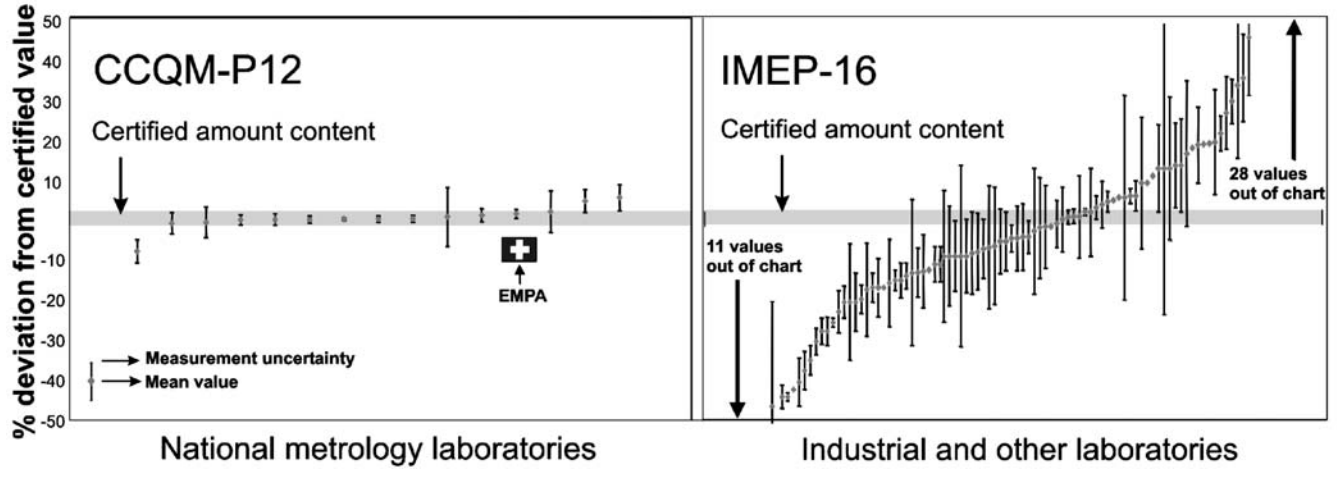

Fig. 4 Display of results as deviations from the certified value for the CCQM pilot study lead in wine and the IMEP results both organised by the IRMM

Conclusion

The main influence contributing to the combined measurement uncertainty is the isotope amount ratio of the blend between sample and spike $u(R_{206,B})$, with the blank value as major component. This implies that apart from isotope amount ratio determinations and accurate mass measurement, the chemical treatment of the sample plays the third important role.

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